

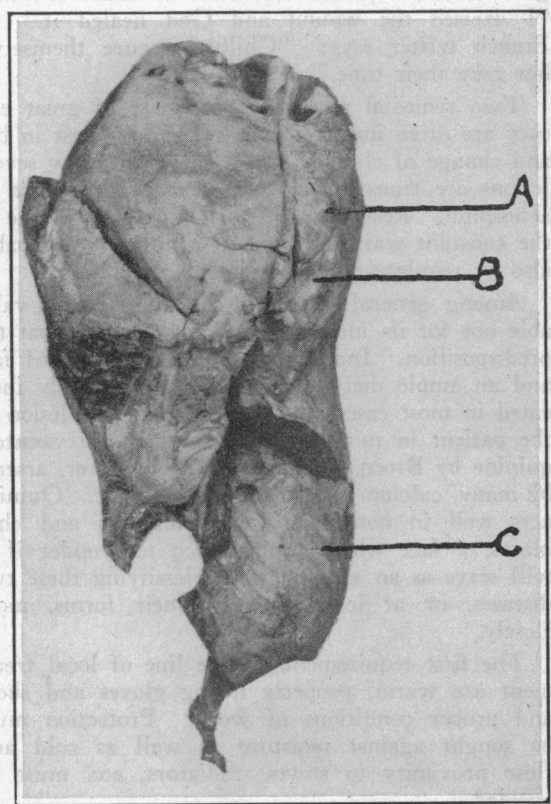
LYMPHOSARCOMA OF THE SUPERIOR MEDIASTINUM.*

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This specimen is from a man 62 years of age, of the superior mediastinum surrounding the great vessels and encroaching upon the heart and lungs.

The duration of symptoms was three years, the first being a pain and soreness behind the right ear which gradually extended to the muscles of the neck on the same side and down the corresponding arm. Next soreness and oppression developed in the chest, accompanied by coldness of the right hand. The patient felt perfectly well except for the pain and occasional disturbance to stomach, latter being relieved by diet. There was no loss of weight up to two years but at the time I saw him there was more or less of a cachetic appearance.

I first saw the patient in July, 1911, and at that time he had the following symptoms:



Pain behind the ear, being more acute in a draft; soreness of the cervical muscles, more marked on the right; lameness in both arms with sensation of cold, more marked on the right; a cough bordering on an aneurismal type, with expectoration of tenacious brownish sputum, the microscope showing pigmented epithelial cells without many bacteria; some soreness in the chest over and to the right of the manubrium, being slightly tender to palpation; and general weakness being very noticeable in the legs. At times there was palpitation of heart, but only upon excitement or strenuous exertion. Patient was well nourished, pupils equal but reacted slowly, right optic disc whiter than the left and sight correspondingly deficient; no noticeable change in vocal cords. There was slight edema of right hand without tender spots, prominence of the jugular veins without pulsation, and small dilated venules of the upper anterior chest wall more marked on the right. Upon percussion the arch dullness was materially increased,

* Read before the San Francisco County Medical Society.

extending about an inch to each side of the sternal border. The heart was in its normal position without murmurs, but at the aortic area two sounds were distinctly heard, the first bordering upon a very soft murmur, being more of a roughened sound, the second accentuated. At the pulmonic area both sounds were heard without murmurs. The abdominal organs were neither enlarged nor tender. Reflexes were present without deviation from normal. The blood pressure on the right arm was systolic 150, left arm 140. The urine and blood were normal except for a slight secondary anemia. Wassermann was negative.

A diagnosis of aneurism of the arch of the aorta was made with question as to tumor and an X-ray picture helped to verify the diagnosis. Under the fluoroscope a distinctly pulsating shadow was found.

From this time on the patient grew worse, edema becoming more marked, extending to the extremities, neck, head and upper part of chest in front and along the mid-axillary line to the crests of the ileum. The lower extremities showed no edema. The last three months the patient was confined to the bed, as this seemed to give the most comfort. Twice while in bed there was exaggerated palpitation of the heart lasting from six to twelve hours, each time leaving him in a weaker condition. Pain in the neck, arms and chest became very intense, and marked tenderness developed in the hepatic region during the last few weeks.

At the time of death the arms were twice the normal size, the left now being the larger. A great amount of edema of both sides of the chest extending down to the iliac crests, a slight edema of the anterior chest wall, face and neck.

The dullness did not enlarge upon percussion, but there developed a distinct systolic murmur and a diastolic shock* over the lesion which so frequently develops in aneurism. There was more or less of an expansile heaving to the chest with slight bulging at the manubrium.

At autopsy the heart was found slightly pushed downward by a large mass which was not only attached to the base of the heart but to the margins of the lungs, trachea and sternum. Upon closer examination the mass was found to be more or less encapsulated and enveloping all the vessels of the heart. The veins were compressed but the arteries remained patent.

The heart showed an old adhesive pericarditis, lungs free except for the marginal attachment to the tumor and metastasis in the liver. Retroperitoneal lymph glands were enlarged, other lymph glands were conspicuously absent.

Section of the tumor shows lymphosarcoma arising probably from the lymph glands with similar structure in a metastatic nodule of the liver.

DEPARTMENT OF PHARMACY AND CHEMISTRY.

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Phylacogens.

The term phylacogen is derived from two Greek words meaning phylaxin-producer. "Phylaxin" is the name applied by Hankin to antitoxin or a defensive proteid found in animals that have acquired an artificial immunity to a given infectious disease. The word phylacogen has been coined to distinguish these new bacterial derivatives from other bacterial therapeutic agents.

The phylacogens are neither bacterial vaccines nor "sera" as commonly understood. They are sterile aqueous solutions of metabolic substances or derivatives generated by bacteria grown on artificial culture media. The bacteria, first killed, are removed by filtration through porcelain.

They are prepared from a variety of pathogenic bacteria—as the several staphylococci, streptococ-

cus pyogenes, bacillus pyocyaneus, diplococcus pneumoniae, bacillus typhosus, bacillus coli communis, streptococcus rheumaticus, streptococcus erysipellatis, etc. The organisms used are of various strains and from cultures derived from various sources. The organisms are present in the material before filtration and dilution, in approximately equal proportions. Thus it will be seen that these products are both "polyvalent" and "mixed." (See Cal. State Jour. Med., April, 1912, p. 167, for definitions.)

The cultures are incubated at 37° centigrade for 72 hours or longer, after which 0.5% phenol is added to the fluid as a preservative. This is then filtered through porcelain. The basic phylacogen made in this manner is used in the preparation of the several specific phylacogens and is called "mixed infection" phylacogen. The specific phylacogens are prepared by adding to this basic material equal amounts of the filtrates obtained by growing and treating the organism considered to be predominant in the pathological condition. For example, in the preparation of typhoid phylacogen, the *b. typhosus* is grown and treated like the several organisms entering into the preparation of the basic phylacogen. The filtrate obtained from the preparation of the typhoid organism alone, is added in equal amount to the basic phylacogen, and the resulting product given the specific name "typhoid phylacogen." These products have been shown to retain their potency for at least two years.

The principle upon which the use of these phylacogens is founded is the theory of multiple infections. It is advanced that practically all acute and many of the chronic diseases are caused by the metabolic products of bacteria; that the human subject is at all times the host of micro-organisms that are pathogenically latent but capable of setting up a diseased process under certain conditions; that the growth of infecting micro-organisms can be arrested and their effects neutralized by products derived from their development in artificial culture media.

It is further advanced that all infections are "mixed" infections; that except in rare instances, there is no such thing as an infection by a single species of micro-organism; that while one species may predominate, the pathological process engendered by it is accelerated and intensified by the presence of organisms of other species—in other words, that in the course of an infectious disease the symptoms are due not only to the effect of a single species of organism (the specific or predominant infection), but to the influence of other organisms whose pathogenic role is not insignificant and which must be reckoned with in any successful scheme of therapeutics.

In accordance with these theories, it is held that certain diseases are objective and subjective symptomatic manifestations of the preponderance in the subject, of the toxic and destructive products of the peculiar species of organism to which the etiology of the disease is ascribed—as for example: *b. typhosus* in typhoid fever; *d. pneumoniae* in pneumonia; *b. tuberculosis* in tuberculosis, etc.; and also that the symptoms are due in part at least, to the destructive material produced by complicating organisms which are always present in great variety and number.

It is advanced that many of the most notable symptoms in pulmonary tuberculosis—such as loss of weight, high temperature, disturbance of circulation, purulent expectoration, destruction of tissue, etc., are due to the complicating organisms, and if the so-called "mixed infection" can be checked or eliminated, efforts may be directed against the *b. tuberculosis* with far greater success than has hitherto been possible in the treatment of this condition.

The phylacogens are administered either subcutaneously or intravenously, the former being the preferred method. The intravenous administration of phylacogen is followed by constitutional reactions much more pronounced than those following the subcutaneous method and in certain cases is decidedly contra-indicated and even dangerous.

The subcutaneous injection of phylacogen is followed by local and constitutional reactions. These may vary in intensity from very slight to quite severe reactions. The usual effect of the subcutaneous injection is a sense of fullness at the site of puncture followed in from one-half to four hours by a chilly sensation which may merge into a distinct chill. In six to twenty-four hours redness and swelling appear at the point of injection, attended with pain, though there may be only tenderness on pressure. Nausea and sometimes an increased number of bowel movements are observed. Frequently there will be numbness around the site of the injection, and at times depression and a pronounced feeling of numbness over the entire body. These phenomena usually pass away in a few hours. Following the reaction the temperature, pulse rate and number of respirations decline and there is a decrease of blood pressure.

The usual effects of intravenous injection are as follows: Within thirty minutes (in some cases one to four hours), the subject feels chilly—a sensation which rapidly becomes more pronounced. He will slip down in the bed, draw the clothing up around the neck, turn over on his side, flex the thighs upon the abdomen, and by this time he will be in a decided chill which will become more and more pronounced until it assumes the proportions of a severe rigor—at times so violent as to shake the bed. This usually lasts from twenty to sixty minutes and gradually passes off. The subject then becomes drowsy, breaking into a profuse perspiration and falling asleep.

Following the reaction, the temperature, pulse rate and number of respirations decline, and there is a decrease of blood pressure as in the subcutaneous method, excepting that these effects come on in a shorter time. As yet, there is no proved scientific explanation of the exact mode of action of these products. It has been observed that those cases respond best which react most strongly to the phylacogens, and there seems to be a direct relation between the vigor of the reaction and the relief of the symptoms.

The usual subcutaneous dose is 5.0 Cc. to 20.0 Cc. daily. It is customary to begin with 5.0 Cc., increasing to 10.0 Cc. on the second or third day.

The usual intravenous dose is 0.5 to 5.0 Cc.—beginning with 0.5 Cc. and increasing gradually to 5.0 Cc. The usual interval between doses is twelve to twenty-four hours—in some instances thirty-six to forty-eight hours.

It would seem that a total disappearance of symptoms does not necessarily indicate a permanent cure, but in common with other forms of bacterial therapy, it is necessary to persist in the treatment and in the employment of adequate dosage.

These products have been employed in the treatment of various acute and chronic infections. Their successful application is dependent, like the bacterial vaccines, upon accurate clinical and bacteriological diagnosis.

To the writer's knowledge but two papers have appeared in current literature, bearing upon this subject. One is to be found in the California State Journal of Medicine, April, 1912, p. 160; and the other in The Therapeutic Gazette, April 15, 1911, p. 257.